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An Approach to Assessing the Influence of Environmental and Occupational Cancer Hazard Identification on Policy Decision-Making

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Background: Cancer hazard identification is critical to informing decisions on preventive actions. However, the influence of cancer hazard assessments on the creation of health-protective regulations is poorly understood. Although prior studies have measured the health and economic benefits of regulatory actions in general, we are not aware of efforts to explicitly study the influence of cancer hazard identification on policy decisions in the United States.

Objectives: In this commentary, we present an approach to examine whether formal identification of a substance as a human carcinogen may prompt a regulatory action to reduce exposure to carcinogens and enhance public health. Further, we discuss the broader implications of cancer hazard identification on policy decision-making, including identifying gaps and providing recommendations.

Methods: Using the Report on Carcinogens (RoC) as a test case, we systematically searched U.S. federal and state databases for notices of regulations mentioning the RoC from 1995 to 2023. For each regulation, we extracted information on the carcinogen(s) regulated, the regulatory agency, the regulatory purpose, the economic sector exposure sources, and the analyzed public health benefits and costs. We created a publicly available, web-based interactive tool to visualize the data.

Discussion: U.S. regulatory agencies have been using cancer hazard evaluations, such as the RoC, for decades to inform public health policy actions to prevent or mitigate cancer risks. Specifically, nonregulatory cancer hazard assessments have been used to prioritize chemical evaluations, support regulatory-based assessments, and trigger regulatory action. Our approach showed that assessing the influence of cancer hazard identification on science-based public health policies is feasible, informative, and needed, and our study is a first step in this direction. We recommend expanding this approach to other cancer and noncancer hazard assessments to ultimately inform our understanding of the influence of hazard classifications on policymaking. https://doi.org/10.1289/EHP12681

Introduction

Cancer is a major public health crisis worldwide. In the United States, 1.9 million new cancer cases and ∼ 600,000 deaths were reported in 2019,[1] of which 42% of newly diagnosed cancers were attributed to modifiable risk factors and could have been prevented.[2] Identification of potential carcinogens, assessment of risk, and mitigation of cancer hazards are vital steps for cancer prevention and protection of public health.

After a carcinogenic hazard is identified, that information may be used by organizations to inform policy decisions to protect public health[3,4] by, for example, triggering a subsequent risk assessment, regulatory activity, or nonregulatory policy.[5] Hazard assessment leading to the identification of carcinogens typically involves a strength-of-evidence determination about the association between the hazard and cancer but not necessarily quantification of the existing level of exposure. Regulatory agencies may rely on cancer hazard identification from one or more authoritative sources, conduct their own assessment to characterize the cancer specific and overall cancer risk or use both methods. They select among possible regulatory or other policy options to reduce the cancer risk and may include a quantitative or qualitative benefit–cost analysis to inform decisions. For example, regulating chemicals under the 2016 Lautenberg Act amendments to the Toxic Substances Control Act (TSCA) requires consideration of available substitutes, costs and benefits, and cost effectiveness.[6] Although there can be considerable time lags between the determination that a substance is a carcinogen and subsequent policy decisions, information in the rulemaking documents or supporting benefits analyses can provide indirect measures of the influence of hazard identification.

Despite the importance of cancer identification, its impact on health-protective regulatory policies is poorly understood. Methodologically, it is difficult to identify metrics that would meaningfully evaluate the impact of these assessments. Public health program evaluation often includes measurable outputs and intermediate outcomes,[7] and limited attempts have been made to evaluate the impact of programs on policy decisions.[8] Although prior studies have measured the health and economic benefits of regulatory actions,[9,10] we are not aware of efforts to explicitly study the impact of cancer hazard identification on policy decisions in the United States.

Our goal is to better understand policy implications of hazard identification, identify areas that need to be strengthened, and offer recommendations to further incorporate the outcomes of science-based cancer hazard evaluations into regulatory decision-making. Using the U.S.-based Report on Carcinogens (RoC)[11] as a test case, we present an approach that begins to examine the link more explicitly between cancer hazard identification and a subsequent regulatory or policy action, which, in turn, is anticipated to yield health and economic benefits. Mandated by the U.S. Congress under Section 301(b)(4) of the Public Health Service Act (PHSA),[12] the RoC identifies and lists agents, substances, mixtures, and exposure circumstances that pose a carcinogenic hazard to a significant number of people residing in the United States. Given its statutory mandate, length of the program, and its 40-y history identifying and listing 256 "known" or "reasonably anticipated" substances to be human carcinogens, we believe the RoC is a good test case for a systematic search.

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Methods

First, we systematically searched federal and state databases for mention of the RoC in published notices of U.S. regulations from 1995 to 2023, then we screened the results for relevant regulatory actions, and finally, we extracted selected information from the regulations and organized the information in our searchable public database (i.e., our tool; Figure 1).

Search Strategy and Eligibility Criteria

We searched for mentions of "Report on Carcinogens" in the Federal Register (FR) (https://www.federalregister.gov/), as well as in supporting materials made available in public dockets for review and comments (https://www.regulations.gov). Although the first RoC listings were published in 1980, we restricted our search to FR publications and associated dockets published since 1995 (Volume 60 onward), when browsing and search capabilities were made available online. The search covered the period of 1 January 1995 through 4 May 2023, the date when the search was last performed.

We limited our query of regulatory materials to documents supporting rulemakings (Document Type = "Proposed Rule" or "Rule" and Docket Type = "Rulemaking") and omitted other types of FR notices. The searches included FR publications and supporting materials (e.g., integrated risk assessments, regulatory impact analyses) because FR notices vary in the level of detail they provide on the justification for a rule or the supporting analyses.

We identified relevant state actions published from 1995 to 2023 (through 4 May 2023) by querying the term "Report on Carcinogens" in state administrative codes and notices of regulatory actions contained in Lexis Advance (https://www.lexisnexis.com/advance). This database includes state registers for all states, Washington, DC, and the U.S. Virgin Islands. We screened the search results to confirm that the state actions cited the RoC, and we excluded any amendments containing duplicated information.

Data Extraction Criteria, Database Creation and Visualization

For each regulation, we extracted information on the agency, publication date, rule stage, regulated carcinogen(s), rule significance, and environmental media or occupational source. We created an interactive web-based database using Tableau software to present the findings in an accessible manner.

Detailed Data Extraction of Specific Actions

We conducted additional, more detailed data extraction for all state actions and a select subset of federal actions. Federal actions with detailed extraction were selected based on criteria that included: *a*) action types that generally have quantitative assessments of costs or benefits, or both, with most of these categorized by the agency as "significant" under Executive Order 12866,[14] as discussed in the FR preamble; *b*) actions that directly address an important exposure pathway (e.g., drinking water), or directly target emission or exposure reductions (e.g., emission standards, categorical discharge limits for major industrial sectors, classes of chemicals), or set occupational exposure limits; and *c*) actions

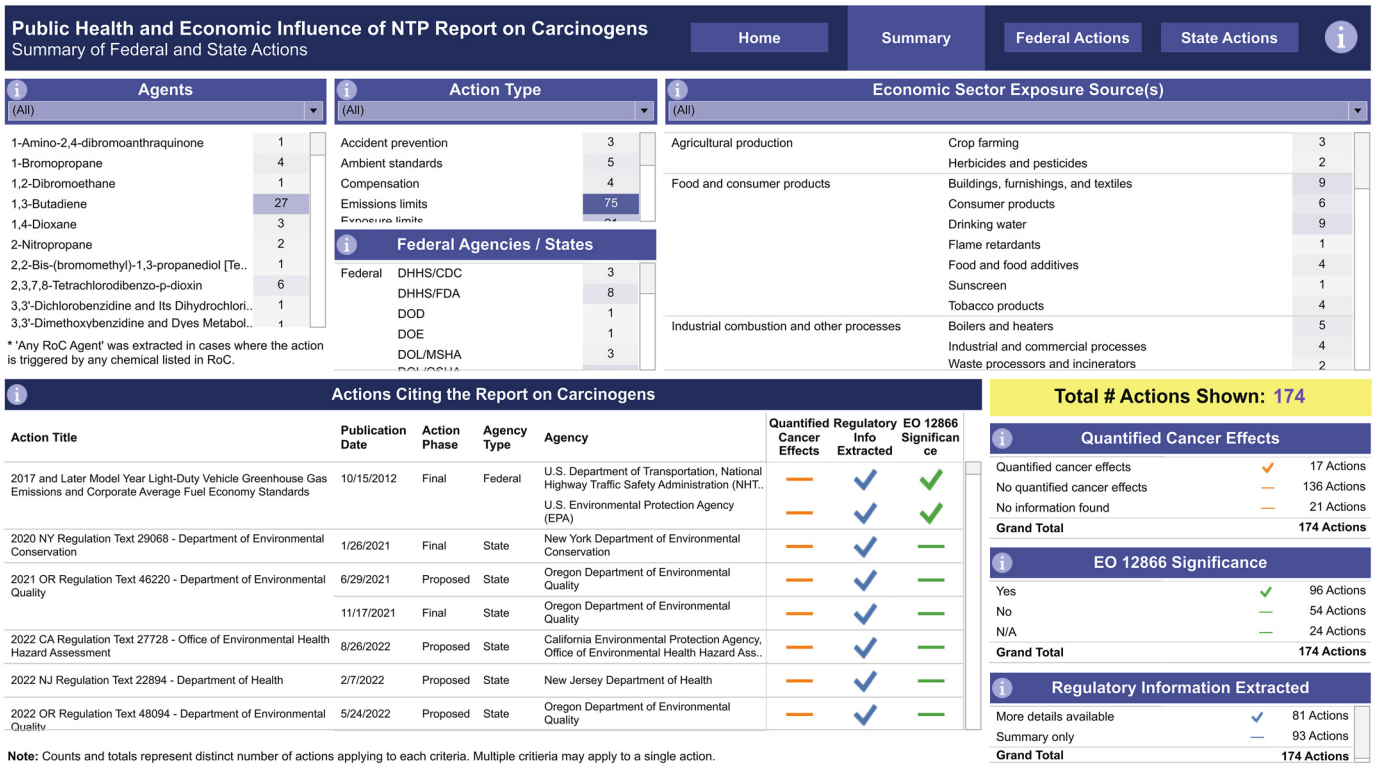

Figure 1. Public Health and Economic Influences of NTP Report on Carcinogens dashboard. This is a thumbnail image of the interactive dashboard[13] that is filterable by agent, action type, agency/state, economic sector exposure sources, quantified health effects (yes/no), Executive Order 12866 significance (yes/no), and regulatory information extracted (yes/no). The numbers (counts) indicate the distinct number of actions that investigated a particular criterion. If an action evaluated multiple agents (top left), action types (top middle), or economic sector exposure sources (top right), an action may be counted in multiple categories. The "Actions Citing the Report on Carcinogens" panel (bottom left) includes each action's title, publication date, stage, publishing agency, whether the action addressed quantified cancer effects, if the action was considered "significant" as defined in Executive Order 12866,[14] or had regulatory information extracted. Note: CA, California; CDC, Centers for Disease Control and Prevention; DHHS, Department of Health and Human Services; DOD, Department of Defense; DOE, Department of Energy; DOL, Department of Labor; EO, executive order; FDA, Food and Drug Administration; MSHA, Mine Safety and Health Administration; NJ, New Jersey; NTP, National Toxicology Program; NY, New York; OR, Oregon; RoC, Report on Carcinogens.

that have in their title substances recognized for their impacts on human health, as indicated by a RoC listing. These selection criteria leave out actions for which detailed quantitative analyses of costs, benefits, or human health impacts are typically not required or produced. For the selected actions, we reviewed the preamble and additional supporting documents, such as the regulatory impact or economic analysis report, to extract details of analyzed costs and benefits.

For regulations with available quantified health benefits (e.g., avoided cancer), we extracted information on the overall costs, quantified public health impacts (e.g., excess cancer deaths avoided), and monetized public health benefits (e.g., estimated U.S. dollar value of avoided cancer cases). If tumor site-specific benefits were quantified for a given agent, we extracted information on quantified measures (e.g., excess lung cancer cases avoided) and monetized benefits (e.g., annual dollars saved from avoided lung cancer cases). The extracted data focused on cancer-related health effects, and therefore, among those for which detailed data were extracted, not all actions had relevant quantified health benefits data. In many instances, the agencies only discussed benefits of avoided cancer qualitatively even when they may have quantified other noncancer health benefits (e.g., reduced asthma hospital visits) or other types of benefits (e.g., climate change mitigation).

Discussion

Our study discusses an approach, using the RoC as an exemplar, to explore the link from cancer hazard identification to policy-making more explicitly. This approach consists of systematic searches and selection of regulatory information using inclusion criteria, detailed data extraction, and an interactive dashboard to explore the data. We relied on only publicly available and searchable regulatory data, and therefore, this study is easily reproduceable and transparent when interpreted by subject-matter experts. Our general approach and tool could be applied to evaluate the impact of other health hazard identification programs, including noncancer effects. From a cancer hazard identification standpoint alone, non-RoC cancer hazard evaluations, including those conducted by the International Agency for Research on Cancer (IARC) and the U.S. Environmental Protection Agency (EPA), were also cited and considered in an agency's decision-making.

Overview of Our Tool

Results from our analysis are provided in an interactive tool[13] consisting of three dashboards—a summary dashboard with metadata from 174 federal and state regulations (Figure 1), and two dashboards with detailed data for all 29 state and 52 federal regulations that allow the user to explore the data on RoC-cited regulatory actions. Metadata includes information, presented in filterable tables, related to *a*) citing or using the RoC in actions (i.e., RoC-listed agents, regulation, and agency/state citing the RoC) and *b*) the purpose of the regulation (i.e., action type, economic sector exposure source) (Figure 1). The federal actions dashboard expands on this information by providing data on the quantified public health benefits, economic benefits, and costs of 52 RoC-relevant regulatory actions. The federal and state dashboards include an overview of the regulatory actions, including RoC impact (available by hovering over the black "i" for each listed action).

Cancer Hazard Listings Cited in Regulatory Actions

The 174 RoC-cited actions are from seven federal executive branch agencies and eight state agencies (Figure 2A). For federal actions, the U.S. EPA accounted for >75% of all citations (112 regulatory actions). Given the U.S. EPA's specific mission to protect human health and the environment by reducing environmental risks using the best available science, as well as the long-standing agency guidelines for evaluating carcinogenic potential of substances in regulatory risk assessment, the disproportionate citing of RoC in regulatory actions was expected. California and New Jersey had the highest number of state actions directly citing the RoC. Figure 2B provides the frequency across agencies of regulatory actions by specific RoC-listed substances. RoC listings associated with the most regulations include benzene, acetaldehyde, formaldehyde, 1,3-butadiene, and naphthalene.

Purpose of RoC-Cited Regulations

Our results identified a diverse array of regulatory actions from several state and federal agencies with differing purposes (Figure 3A) and regulated exposure sources (Figure 3B). The most common federal and state actions cite the RoC to protect public health by setting emission and exposure limits, restricting trade or use, and communicating hazards (Figure 3A) in numerous economic sections (Figure 3B). The purpose of approximately two-thirds ($N = 77$) of the U.S. EPA regulations was to limit either emissions ($N = 67$) or harmful exposures ($N = 10$), whereas communicating hazard was a predominant purpose ($\sim 50\%$) for actions by the Department of Labor (DOL) and by states. Regulations to limit emissions were primarily in the manufacturing and transportation economic sectors. Actions setting exposure limits were mainly for workplaces, foodstuffs, and consumer products. Of the federal regulations to limit trade or use of substances $\sim 75\%$ were published by the U.S. EPA. These included regulations for new uses, which typically fall under TSCA Significant New Use Rules (SNURs) (e.g., benzidine-based chemicals, asbestos),[15,16] or for specific current applications (e.g., trichloroethylene, polybrominated biphenyls).[17–19]

Many regulations for which the RoC was cited in the notice or supporting material were promulgated under the authority of programs and legal authorities, and thus the sources and purpose reflect the agency purview. Examples from the U.S. EPA to limit emissions, exposure levels, or restrict trade include the Clean Air Act (CAA), the Clean Water Act (CWA), the Safe Drinking Water Act (SDWA), the TSCA, the Emergency Planning and Community Right-to-Know Act (EPCRA), and the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA).[20–24] These regulations have demonstrated success in preventing adverse health effects from exposures to environmental pollutants and in enhancing public health. For example, retrospective and prospective analyses of CAA regulations have quantified the air quality improvements and significant health benefits realized since the passage of the law.[25–27]

Several states and federal agencies use the RoC as an authoritative source for information on cancer hazard identification in their decision-making processes and communication of these hazards to workers and the public. DOL's Occupational Safety and Health Administration's (OSHA) and Mine Safety and Health Administration's (MSHA) Hazard Communication Standards apply to any RoC agent to require hazard labeling, distribution of safety data sheets to employees, and employee training (i.e., any chemical listed in the RoC triggers regulatory requirements). For example, our search identified 10 RoC-cited actions subject to California's Safe Drinking Water and Toxic Enforcement Act, known as Proposition 65, which requires specific labeling. Similarly, our search found two New Jersey and four Massachusetts actions subject to state-specific worker and community right-to-know laws that use the RoC. U.S. EPA regulations related to hazard communication for specific substances include those promulgated under the TSCA or codified under the EPCRA and Pollution Prevention Act and require adding RoC-listed carcinogens (e.g., dioxins and the

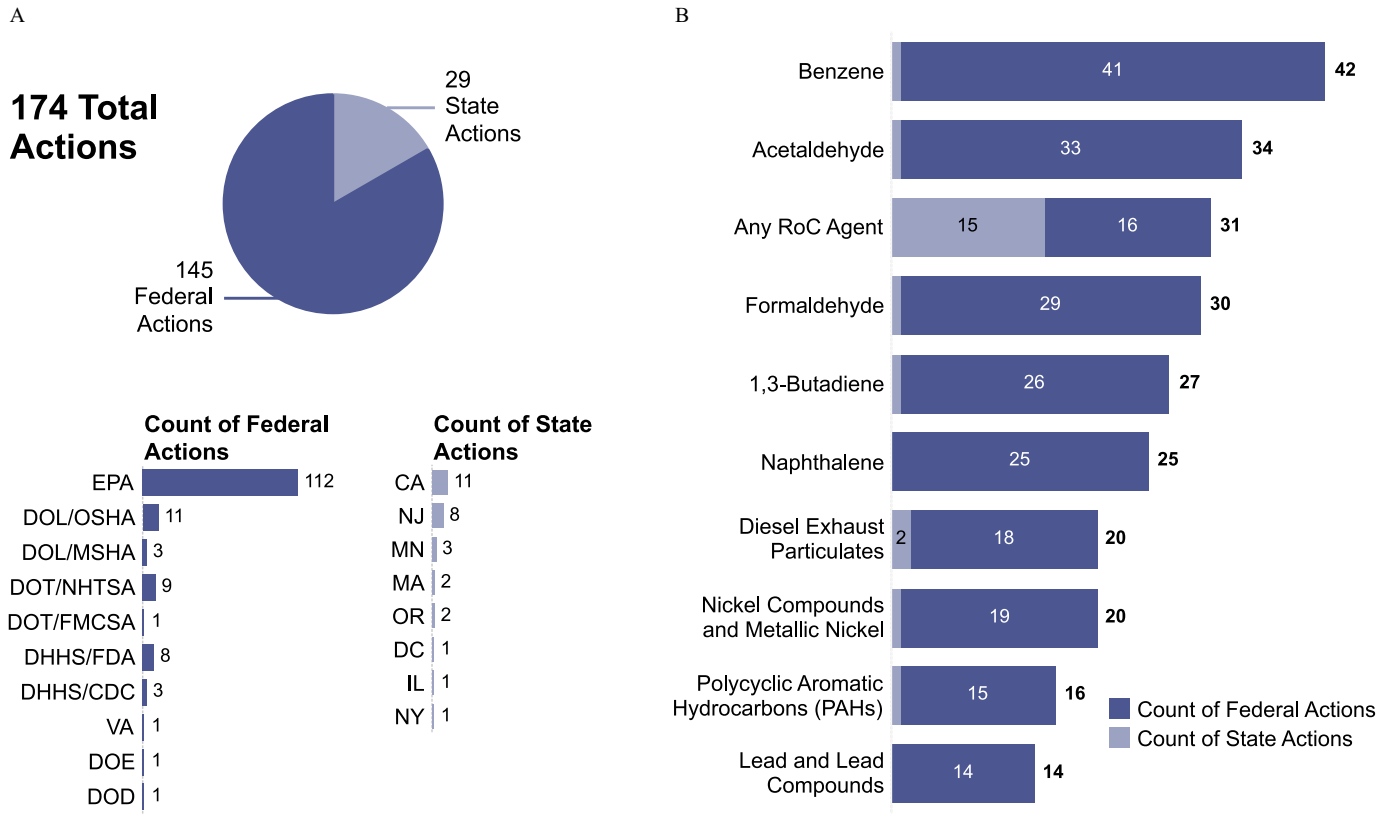

Figure 2. Report on Carcinogens (RoC)-cited listings: federal and state actions citing the RoC. (A) Proportion of federal and state actions, with a display of action counts for specific federal agencies and states citing the RoC. (B) The 10 most addressed RoC listings among 121 distinct actions (70% of total actions). Counts include both proposed and final regulatory actions. See the interactive dashboard[13] for the frequency of citations for all RoC-listed substances. All counts shown represent distinct numbers of actions associated with the accompanying criteria. In (A), five actions were produced jointly by the U.S. EPA and DOT and are included in both counts. In (B), we note that many actions address more than one RoC agent and are included in multiple bar totals. In (B), "Any RoC Agent" was assigned in cases where the action is triggered by any chemical listed in RoC. Note: CA, California; CDC, Centers for Disease Control and Prevention; DC, District of Columbia; DHHS, Department of Health and Human Services; DOD, Department of Defense; DOE, Department of Energy; DOL, Department of Labor; DOT, Department of Transportation; EPA, Environmental Protection Agency; FDA, Food and Drug Administration; FMCSA, Federal Motor Carrier Safety Administration; IL, Illinois; MA, Massachusetts; MN, Minnesota; MSHA, Mine Safety and Health Administration; NHTSA, National Highway Traffic Safety Administration; NJ, New Jersey; NTP, National Toxicology Program; NY, New York; OSHA, Occupational Safety and Health Administration; OR, Oregon; VA, Department of Veterans Affairs.

dioxin-like compounds, 1-bromopropane, 1,4-dioxane) to the U.S. EPA's Toxic Release Inventory (TRI).

Public Health and Economic Benefits of RoC-Cited Regulations

A unique aspect of our method is its detailed examination of individual RoC-cited regulatory actions for which agencies quantified economic (monetized benefits) or public health (avoided adverse cancer health effects) estimates from exposure to a listed substance(s) ($N = 11$; Table 1) or from a source [$N = 5$ the U.S. EPA National Emissions Standards for Hazardous Air Pollutants (NESHAP); Table S1].

Seven proposed or final substance-specific regulatory actions by the OSHA, the MSHA, and the U.S. EPA protect workers from occupational diseases by *a*) setting occupational exposure standards (beryllium, hexavalent chromium, crystalline silica, and dichloromethane), *b*) banning or restricting use (two specific workplace uses of trichloroethylene, asbestos, and dichloroethane), and *c*) communicating hazards (OSHA and MSHA rules for any RoC-listed agent) for chemicals listed in the RoC (Table 1). Except for the asbestos regulation ($1,000/y, based on restricting new uses), the quantified monetized benefits from these worker-related regulations ranged from $9 million to >$8 billion/y. The formaldehyde emissions regulations protect workers and users from consumer and industrial products ($24 million–$66 million in annualized benefits). The five NESHAP regulations with monetized benefit–cost or avoided cancer analyses (Table S1) control the emissions of multiple substances listed in the RoC from waste combustors, ferroalloy emissions citing RoC's nickel listing, and technology reviews of surface coating for wood products (RoC-cited listing of formaldehyde, acetaldehyde, and nickel), nutritional yeast manufacturing (RoC-cited listing of acetaldehyde), and paper and pulp combustion sources (RoC-cited listing of acetaldehyde, naphthalene, and nickel).

Ninety-six (66%) of the 145 proposed and final federal regulatory actions were identified as "significant" under Executive Order 12866[14] and were required to undergo an Office of Management and Budget review, including an assessment of the potential costs and benefits. "Significant" rules include those actions expected to have at least a $100 million impact on the economy or to raise novel legal or policy issues.

Approach Limitations

We note limitations to the utility of our approach. Given the limited number of regulations identified that quantified benefits, it is highly likely that we greatly underestimated the downstream economic impact of the RoC. We note that RoC only identifies carcinogenic hazards; agencies conduct their own risk assessment and

A

Distinct Count of Actions: 1 – 67

Action Type	Federal Actions / Agency: EPA	DOL/OSHA	DOL/MSHA	DOT/NHTSA	DHHS/FDA	DOD	DOE	All State Actions	Total Count of Actions
Emissions limits	67			9				4	**75**
Hazard communication	10	5	1		2			16	**34**
Exposure limits	7	5	2		1		1	5	**21**
Trade/use restrictions	12				3	1		1	**17**
Total Count of Actions	**94**	**10**	**3**	**9**	**6**	**1**	**1**	**26**	**145**

B

Distinct Count of Actions: 1 – 26

Action Type	Exposure Source Category: Other/general	Manufacturing releases	Occupational	Transportation	Food and consumer products	Mining, quarrying, and oil and gas extraction	Industrial combustion and other processes	Utilities (power, water, and waste)	Agricultural production	Total Count of Actions
Emissions limits	18	26	3	25	3	8	6	4		**75**
Hazard communication	23	1	12		4	1	2		1	**32**
Exposure limits	6	3	12	1	8	4		1		**21**
Trade/use restrictions	5	9	8	1	10					**17**
Total Count of Actions	**50**	**39**	**35**	**27**	**25**	**13**	**8**	**5**	**1**	**143**

Figure 3. Action purposes, agencies, and types. (A) 145 distinct actions (83% of total actions) address the top four purposes of regulatory action, categorized by federal agency or state. (B) 143 distinct actions (82% of total actions) addressing the top four regulatory action purposes, categorized by major exposure source groupings. Counts include both proposed and final regulatory actions. See the interactive dashboard[13] for the frequency of citations for all action types and exposure sources. All counts shown represent distinct numbers of actions associated with the accompanying criteria. Seven additional action types are excluded from this visual. In (A), three federal agencies are excluded because they addressed only purposes also excluded. Five actions were produced jointly by the U.S. EPA and DOT and are included in both (A) and (B). Some actions address more than one exposure source and/or purpose and are included in multiple totals in both (A) and (B). In (B), "Other/general" describes specific exposure sources that did not fit into other existing exposure categories. Note: FDA, Food and Drug Administration; DHHS, Department of Health and Human Services; DOD, Department of Defense; DOE, Department of Energy; DOL, Department of Labor; DOT, Department of Transportation; EPA, Environmental Protection Agency; MSHA, Mine Safety and Health Administration; NHTSA, National Highway Traffic Safety Administration; OSHA, Occupational Safety and Health Administration.

economic analyses for rulemaking, including dose–response estimation. Our method also highlights the potential disconnect between cancer hazard identification and quantified benefits. In some cases, benefit analyses may focus on pollutants and health effects for which quantification methods are readily available and sufficient to justify regulations (e.g., particulate matter) and discuss cancer benefits only qualitatively. In others, they may not quantify other benefits, such as those realized from reducing exposure to RoC-listed carcinogens even when such carcinogens are targeted either by the rule directly or as part of a mixture of pollutants.

Actions reported by regulatory sources may mitigate multiple hazards and may not adequately capture each substance within a complex mixture of potential exposures. We attempted to evaluate the supporting documentation for each regulatory action for further detail on the specific RoC substances, but other regulated coexposures and mixtures may exist that were not identified. We noted differences in the extent to which the RoC was used to support the regulation. For some actions (e.g., the U.S. EPA's SNUR for toluene diisocyanates and related compounds)[28] the RoC was merely cited among the multiple justifications for pursuing the rule. In other instances, the RoC tumor site conclusions were used in analyses to support the rule.

Our data extraction identified variations in the type and breadth of supporting information for regulations across unique statutory authorities, possibly reflecting differences in statutory factors for regulatory decisions and in rulemaking practices across programs and agencies. For instance, the CAA requires only a justification of public health benefits and does not require consideration of costs or technical feasibility when setting ambient air quality standards or promulgating regulations under certain CAA authorities.[29] This, in turn, may place a greater weight on certain aspects of the risk assessment and risk management processes. We also note that there is a general lack of consistency in how much hazard information is included and where that information is reported (e.g., FR notice vs. supplemental/background information).

How Authoritative Cancer Hazard Assessments Are Used in Regulatory Actions

Given the limited utility of our initial search to fully uncover the multifaceted considerations that go into a regulatory action, our approach requires a deeper dive to understand how hazard assessments were used by the regulatory agencies. In addition to directly citing the RoC, most regulatory actions also cite other authoritative sources, such as the IARC and the U.S. EPA. Our utilization of the U.S.-based RoC as a search test case may serve as a proxy, albeit imperfect, for cancer hazard evaluations overall. A detailed analysis is not possible with every regulatory action and may be impossible without intimate knowledge of each rulemaking process and history. Therefore, we highlight a few case examples (e.g., substance-specific regulations) to better understand how authoritative reviews

Table 1. Substance-based regulations monetized benefit–cost analysis or avoided cancers.

Substance/how cited	RoC listing	Agency/regulation	Monetized action public health benefits[a]	Quantified cancer prevention benefits
Any RoC listing[b] MSHA requires mining operators to use RoC as one of its criteria for evaluating health effects	Known or reasonably anticipated to be a human carcinogen (RAHC)	MSHA Hazard communication (HazCom) (2002)	Not reported	Annual cancer deaths avoided: • 50 between years 11 and 20 • 9.4 after year 20
Any RoC listing[b] RoC is a source for identifying cancers	Known or RAHC	OSHA Hazard communication standard modification (2012)	Cancer and noncancer $250,000,000 (7% DR)	Not reported (analysis did not separate out estimates of cancer effects)
Asbestos RoC cited in supporting materials	Known to be a human carcinogen Lung cancer and mesothelioma[c] First listed in the 1st RoC (1980)	U.S. EPA Proposed regulation of certain conditions of use under Section 6(a) of the Toxic Substances Control Act (TSCA) (2023) Restricted new use	Cancer $1,167–$1,169 (7% DR)[d] $3,058–$3,062 (3% DR)	Not reported[e]
Beryllium and beryllium compounds RoC cited in rule notice to support health effects and respond to comments	Known to be a human carcinogen Lung cancer Listing changed from RAHC (1981) to known in the 10th RoC (2002)	OSHA Occupational exposure to beryllium (2017) New permissible exposure limits	Cancer and noncancer $267,292,508 (7% DR) $601,864,185 (3% DR)	4 annual fatal lung cancers
Chromium hexavalent compounds RoC cited in rule notice to describe events leading to the final rule, support health effects	Known to be a human carcinogen Lung cancer First listed in the 1st RoC (1980)	OSHA Occupational exposure limit for hexavalent chromium (2006) Revised existing exposure standard	Tumor-specific benefit $36,000,000–$504,000,000 (7% DR) $112,000,000–$896,000,000 (3% DR)	Lung cancer deaths • 1,782–6,546: 45 y lifetime working • 40–145: annual Non fatal cancers • 5–20: annual
Dichloromethane RoC cited in rulemaking	RAHC Liver and lung cancer (animal studies) First listed in the 5th RoC (1989)	U.S. EPA Methylene chloride; rulemaking under TSCA Section 6(a) (2023) Limit emissions and exposure, restrict use, establish exposure limit	Cancer and noncancer $13,400,000–$13,900,000 (7% DR) $17,000,000–$18,500,000 (3% DR)	Not reported[e]
Silica, crystalline (respirable size) Cited RoC in rule notice to describe events leading to the final rule, support science, and respond to comments	Known to be a human carcinogen Lung cancer Listing changed from RAHC to known in the 9th RoC (2000)	OSHA Occupational exposure to respirable crystalline silica (2016) Amend standards for occupational exposure	Cancer and noncancer $4,811,814,147 (7% DR)[f] $8,686,913,216 (3% DR)	Lung cancer • 65–183: annual • 2,921–8,426: lifetime (45 y)
Formaldehyde RoC cited in final rule notice and supporting documents to support cancer findings, benefits, and respond to comment	Known to be a human carcinogen Nasopharyngeal cancer Myeloid leukemia Sinonasal cancer Listing changed from RAHC (1981) to known in the 12th RoC (2011)	U.S. EPA Formaldehyde emission standard for composite wood products (2016) Reduce formaldehyde emissions	Cancer $24,000,000–$66,000,000 (7% DR) $62,000,000–$171,000,000 (3% DR)	Nasopharynx cancer 26–65: annual
Trichloroethylene RoC cited in final rule notice and supporting documents	Known to be a human carcinogen Listing changed from RAHC (2000) to known in the 14th RoC (2016) Sufficient: kidney cancer Limited: non-Hodgkin lymphoma	U.S. EPA Trichloroethylene: regulation of use in vapor degreasing under TSCA Section 6(a) (2017) Proposed rule Trichloroethylene: regulation of certain uses under TSCA Section 6(a) (2016) Proposed rule	Cancer Total $169,000,000 (7% DR) $311,000,000 (3% DR) $31,000,000–$227,000,000 (7% DR) $65,000,000–$446,500,000 (3% DR) $4,500,000–$12,800,000 (7% DR) $9,300,000-$25,000,000 (3% DR)	18.8–113: cancer cases 0.7–1.6: kidney 1.4–3.2: non-Hodgkin lymphoma

Note: DR, discount rate; EPA, Environmental Protection Agency; MSHA, Mine Safety and Health Administration; OSHA, Occupational Safety and Health Administration; RoC, Report on Carcinogens; TSCA, Toxic Substances Control Act.
[a]Agencies generally use 3% and 7% discount rates when reporting costs and benefits, consistent with Office of Management and Budget guidance; the table provides annualized values.
[b]Any RoC refers to actions that are triggered by any chemical listed in the RoC. Benefits in these hazard communication rules are derived from avoided chemical exposure in the workplace and the resulting acute or chronic effects.
[c]Listing based on lung cancer and mesothelioma; now associated with several cancer sites.
[d]Small monetary benefits are due to few exposed workers (<500 workers) and consumers (~400 people) for the new restricted uses.
[e]Analysis does not estimate number of cancer cases or excess deaths but instead reports the reduction in microrisk of cancer per exposed individual.
[f]Large monetary benefits are due to the significant number of avoided illnesses and excess deaths.

are being used. We found that regulatory agencies used cancer hazard identification in several different ways, including *a*) potentially triggering regulatory action, *b*) prioritizing or leading to the agency initiating a regulatory evaluation, and *c*) supporting the cancer hazard assessment in a regulatory action.

- **Potentially triggering regulatory action.** Although the RoC is not a regulatory document, certain federal and state regulatory agencies have chosen to base specific regulatory actions on the listing of a substance in the report (as described above). Similarly, cancer hazard listings from other authoritative bodies, such as the IARC, may be impetus for action. We highlight important state and federal cancer hazard communication standards to workers and to the public, a U.S. EPA action prohibiting ocean dumping of materials containing carcinogens, and reporting requirements of carcinogens above a *de minimis* concentration level for exporting or to the TRI.[11] These regulations can result in significant monetary health benefits; for example, the OSHA hazard communication standard quantified $250 million in cancer-related benefits (Table 1).[30]
- **Prioritizing or initiating a regulatory evaluation.** In some instances, cancer hazard conclusions were found to be used early in regulatory decision-making, including prioritization of chemical hazards for risk evaluations. For example, the U.S. EPA's process for assessing chemicals under the TSCA uses authoritative cancer hazard assessments, including the RoC, to identify potential candidates for review in a stepwise prioritization plan. Our review of three OSHA regulatory actions with quantified health effects [beryllium and beryllium compounds (beryllium), hexavalent chromium compounds (chromium), respiratory crystalline silica (silica)] suggests that identifying substances as carcinogens were significant events leading up to the rulemakings.[31–33] Occupational exposure limits for these chemicals were first established in 1971 based on noncancer outcomes. Following the national and international recognition of these substances as known human carcinogens from 1980 to early 2000, unions and public health organizations petitioned or sued the OSHA to develop emergency standards, prioritize hazards, and evaluate enforcement. The OSHA conducted its evaluation leading to the three revised occupational exposure limits to protect workers from cancer and noncancer outcomes.[31–33]
- **Supporting the cancer hazard assessments.** Although the OSHA conducts independent hazard evaluations, external authoritative hazard conclusions, such as the RoC and IARC assessments, support the determination of significant risk and defend the science. For example, the silica rule[32] repeatedly references the RoC (Table 1), especially in response to public comments. In the discussion regarding whether the scientific literature is false, the OSHA stated it placed the "greatest weight" on conclusions from the RoC and IARC assessments, indicating that the carcinogenicity of crystalline silica has been "well established." In similar instances, the U.S. EPA cited the RoC in response to public comments to address specific scientific issues and the quality of findings from individual studies and to support carcinogenicity. Finally, the U.S. EPA and OSHA reference authoritative cancer hazard assessments for the cancer sites used in the benefit–cost analysis.

For other substance-specific regulations, such as the U.S. EPA's proposed rulemakings on trichloroethylene, asbestos, and methylene chloride,[18,34,35] the specific use of the RoC is less clear given that the rules mainly cite the RoC for its cancer conclusions. Other cancer hazard evaluations, such as IARC assessments, may play a greater role in these rules.

State and federal agencies may separately document nonregulatory science-based hazard and risk assessment from rulemaking, and thus, it is possible that cancer hazard evaluations may influence regulation indirectly (e.g., prioritizing chemicals for review, providing information in an internal assessment). One example is the U.S. EPA's Integrated Risk Information System (IRIS) program, which conducts an independent risk assessment to inform U.S. EPA regulatory action. To further understand the role of external cancer hazard evaluations in U.S. EPA IRIS assessments, we reviewed 47 IRIS assessments available for ∼62 RoC-listed chemicals regulated by the 112 U.S. EPA actions. Most RoC listings predated the IRIS assessments (>90%), suggesting that RoC listings could have direct (e.g., being cited as support for carcinogenicity and, thus, the need for regulation) and indirect effects (e.g., prioritizing agents for review or informing the assessment) on the actions. We are not able to evaluate whether the RoC influenced chemical prioritization, and complete toxicological summaries were only available for a subset of listed chemicals. The toxicological reports provide some support for external cancer evaluations, such as the IARC (and, to a lesser degree, the RoC) being cited by IRIS assessments, which were primarily to support IRIS conclusions. Unfortunately, given the limited information about internal deliberations during regulatory development and sometimes convoluted pathways to decision-making, the indirect influence of the RoC is unknown and likely uncapturable. There are very likely more regulatory actions of RoC-listed carcinogens beyond those that have been identified through our approach.

Recommendations

We offer the following suggestions to further elucidate the influence and effectiveness of hazard identification conclusions on regulatory decision-making:

- Collaborate across federal and state regulatory agencies to promote greater consistency and transparency for presenting independent hazard conclusions and how they were considered in decision-making, particularly if used as a primary justification for the action. This includes citation of all hazard conclusions from authoritative bodies if applicable and relevant to the rule. Doing so will increase transparency in regulatory decision-making to the public and allow for greater uniformity and interpretability across actions.
- Use subject-matter expertise to better understand the complete picture, including nuances, of how health hazard identification may influence policies. Our initial step assessed direct citations as a metric for the influence (or lack thereof) of the RoC on decision-making. However, we found that our conclusions are not necessarily captured in searchable documents (e.g., U.S. EPA's Integrated Science Assessments for criteria air pollutants, Agency for Toxic Substances and Disease Registry Toxicological Profiles, and the U.S. EPA's TSCA Section 5) even when they might have been considered as part of an impactful nonregulatory scientific conclusion by an agency that was then relied on for regulatory decision-making. In other instances, actions were updates or offshoots of previous rules, for which a direct line from a hazard conclusion becomes impossible without intimate historical knowledge. This may be intentionally done by a state or federal agency to focus on the action in the most succinct and efficient manner possible. Last, authoritative cancer hazard conclusions may have been used in prioritization exercises to determine whether policy action is needed.
- Continue to advance methodologies to more robustly monetize public health benefits associated with prevention and/or mitigation of carcinogenic risks, particularly when an economic analysis is required to support a rulemaking.
- Expand monetization of noncancer health outcomes in economic analyses. We also acknowledge a recognized gap in

practice is the consideration of noncancer health outcomes in benefit–cost analysis.[10,36]
- Encourage other research-based organizations producing cancer and noncancer hazard assessments or conducting primary research studies to routinely evaluate their program's influence on policy using methods similarly in this commentary.

Conclusions

As evidenced by the War on Cancer[37] and the Cancer Moonshot 2.0,[38] cancer prevention begins with identifying carcinogenic hazards. We provide a first effort consisting of a transparent, measurable, modifiable, and stepwise approach to link hazard identification and policy decision-making. We learned that the RoC has been extensively used for >25 y to inform U.S. regulatory actions. Further, cancer hazard conclusions from multiple authoritative bodies may lead to regulatory action, although the time to policy action to protect public health may be considerable. Expansion of our concept to other cancer and noncancer hazard assessments would allow for a more comprehensive evaluation of the impact and relative contribution of hazard identification to regulatory decision-making. We acknowledge that hazard identification is only one piece of information used to inform regulatory decisions and is part of the complex paradigm of translational research to policy in environmental health sciences.[39] As such, our method should be considered in the context of the broader policymaking process. In addition, improving current methods, including examining the timing of policy decisions in relation to publication about hazard, and complementing these analyses with qualitative data (e.g., interviews) may ultimately improve our understanding of the effectiveness of science-based hazard identification in shaping public health policies.

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